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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,823	02/12/2002	Waldemar Debinski	6460-41	8785

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/075,823	**Applicant(s)** DEBINSKI ET AL.	
	Examiner Phuong Huynh	**Art Unit** 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11 August 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1,9-14 and 18*.
   Claim(s) withdrawn from consideration: *2-8 and 19-43*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 5. Applicant's reply has overcome the following rejection(s): the rejection of claims 1 and 9 under 35 U.S.C. 112, second paragraph is hereby withdrawn in view of the amendment to said claims.

Continuation of 11. does NOT place the application in condition for allowance because:

Claims 1, 9-11, and 13-14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 6,235,713 B1 (of record, filed Aug 1997; PTO 892) in view of US Pat No. 5,874,290 (of record, Feb 1999; PTO 892), Hamel et al (Acta Neurochirugica 142: 113-138, 2000; PTO 892), Wesseling et al (J Neurosurg 81(6): 902-9, Dec 1994; PTO 892) and Amalfitano et al (Cancer Genet Cytogenet 116: 6-9, 2000; PTO 892).
Applicants' arguments filed 8/11/06 have been fully considered but are not found persuasive.
Applicants' position is that the '209 patent does not teach or disclose the molecule detected in fetal brain tissue is VEGF-D. The '713 patent does not teach or disclose the detection of full-length native VEGF-D. Wesseling et al do not teach or disclose the detection of full-length native VEGF-D.

In response, none of the pending claims recite "fetal brain tissue". The glioblastoma multiforme is derived from tumor brain tissue as taught by the '290 patent. In fact, the specification discloses diagnosing and treating malignant tumors including, in particular, brains cancers such as GBM, which is glioblastoma multiforme (see page 6, line 25). The '713 patent teaches a method of detecting VEGF-D. This rejection would have been under 35 U.S.C 102(b) had the '290 patent teaches the molecule detected in brain tissue is VEGF-D. The '713 patent teaches a method of detecting VEGF-D in a biological sample comprising the steps of contacting the sample with a probe such as labeled monoclonal antibody that binds specifically to the native full length human VEGF-D (see col. 6, lines 66-67 bridging col. 7, lines 1-7, col. 5, lines 51-67, in particular). The reference VEGF-D is a native VEGF-D protein (see col. 19, lines 34-42, VEGFD full FLAG, in particular) and could be proteolytic cleaved to form the VEGF-D homology domain (see col. 19, line 25, VEGFD delta N deltaC, in particular). Wesseling et al teach human glioblastoma mulitforme while Amalfitano et al teach human glioblastoma multiforme cell exhibits abnormal ploidy for chromosome X. Thus the combined teachings of the references disclose the detection of full-length native VEGF-D using antibody to full-length human VEGF-D as taught by the '713 patent in the human brain tissue such as glioblastoma multiforme as taught by the '290 patent, Wesseling et al and Amalfitano et al.

Claims 12 and 18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 6,235,713 B1 (of record, filed Aug 1997; PTO 892) in view of US Pat No. 5,874,290 (of record, Feb 1999; PTO 892), Hamel et al (Acta Neurochirugica 142: 113-138, 2000; PTO 892), Wesseling et al (J Neurosurg 81(6): 902-9, Dec 1994; PTO 892) and Amalfitano et al (Cancer Genet Cytogenet 116: 6-9, 2000; PTO 892) as applied to claims 1, 9-11, and 13-14 and further in view of Achen et al (of record, Eur. J. Biochem. 267: 2505-2515, May 2000; PTO 1449).

Applicants' arguments filed 8/11/06 have been fully considered but are not found persuasive.
Applicants' position is that there is no teaching in the references, alone or in combination that show that the antibody binds to VEGF-D detected in the human glioblastomas of instant application. Achen et al, standing alone or in combination teach the detection of a native VEGF-D homology domain in brain cancer. None of the references teach the detection of VEGF-D in the brain nor, was the form of VEGF-D in the brain known prior to applicants invention.

In response, Achen et al teach various monoclonal antibodies such as VD1, VD2, VD3 and VD4 that bind specifically to the homology domain of human VEGF-D (see page 2507, col. 2, Results, production of anti-VEGF-D mAbs, page 2508, col. 2, last paragraph, in particular). Achen et al teach antibody such as VD2 also binds to the native VEGF-D protein (see page 2508, col. 2, in particular) and the VEGF-D homology domain (see page 2511, col. 1, in particular). Achen et al teach the reference antibody could block the mitogenic response of vascular endothelial cells to VEGF-D (see page 2512, col. 1, in particular) and strongly inhibits the binding of VEGFDDNDC or the VEGF-D homology domain (VHD) to both VEGFR2 and VEGFR3 (see page 2511, col. 1, last par, in particular). Achen et al teach that these antibodies are useful for analyzing angiogenesis induced by VEGF-D and its contribution to metastatic spread (see page 2513, col. 1, last paragraph, in particular). In fact, the antibody VD1 for detecting native protein VEGF-D homology domain used by applicant is from Achen et al, see page 32, lines 29-30. The brain cancer used by applicant is a cell line from glioblastoma multiforme, see specification page 32, line 18. Wesseling et al teach human glioblastoma mulitforme while Amalfitano et al teach human glioblastoma multiforme cell exhibits abnormal ploidy for chromosome X. Thus the combined teachings of the reference disclose the detection of full-length native VEGF-D using antibody to full-length human VEGF-D as taught by the '713 patent in the human brain tissue such as glioblastoma multiforme as taught by the '290 patent, Wesseling et al and Amalfitano et al. The '290 patent also teaches glioblastoma multiforme cell line as well as tumor tissues (see col. 25, lines 55, col. 43, lines 35-62, in particular). As such, the combined teachings of the references teach the claimed invention.

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